receptor molecules form homo- (RXR-RXR) and heterodimers (RAR-RXR) that act as transcription factors. These dimers bind to specific *cis*-regulatory sequences in the promoters of retinoid-responsive target genes, termed RARE (Retinoic Acid Response Elements), regulating their transcription.

A RARE sequence has a minimal half-site consensus sequence that is generally well conserved as AGGTCA or AGTTCA (Mangelsdorf *et al.*, 1994, "The retinoid receptors," *in*: The Retinoids: biology, chemistry, and medicine, Sporn *et al.*, eds., New York: Raven Press, pp. 327-331). RAREs are typically configured into one of three structured motifs: direct repeats, palindromes, and complex elements without an obvious consensus structure. The direct repeat requires a lesser amount of receptor to activate a retinoid-inducible gene than the other configurations. In addition, direct repeats separated by 5 nucleotides have demonstrated the strongest responses while moderate responses are typically generated by direct repeats separated by 2 nucleotides. (See Mangelsdorf *et al.*, 1994, "The retinoid receptors," *in*: The Retinoids: biology, chemistry, and medicine, Sporn *et al.*, eds., New York: Raven Press, pp. 327-331.)

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The resulting changes in gene expression are caused either directly by retinoid receptor regulation of target gene expression, or indirectly through the action of retinoid-activated signal transduction pathways, *for example*, pathways activated by the transcription factor AP-1. These gene expression changes are ultimately responsible for the growth-inhibitory effect of retinoids (Warrell, *Id.*).

Please replace the paragraph at page 11, line 24 to page 12, line19, with the following paragraph:

Another advantage of such compounds is that they can be expected to have a growth-inhibitory effect without producing systemic side effects found with other growth-inhibitory compounds known in the prior art. For example, many growth-inhibitory drugs and compounds known in the prior art disadvantageously induce p21 gene expression, which induces senescence, growth arrest and apoptosis by activating a plurality of genes, the expression of which is associated with the development of diseases, particularly age-related diseases such as Alzheimer's disease, atherosclerosis, renal disease, and arthritis (as disclosed in co-owned and co-pending U.S. Serial No. 60/265,840, filed February 1, 2001

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and U.S. Serial No. 09/861,925, filed May 21, 2001, incorporated by reference herein, Retinoic acid-induced growth inhibition in MCF-7 cells, in contrast, does not induce p21 (Zhu *et al.*, 1997, *Exp. Cell Res.* 234:293-299). The genes identified herein that are induced by retinoids are not known to be associated with any disease or disadvantageous or pathogenic effect when expressed in an animal. Thus, identification of such compounds that mimic the growth-inhibitory effects of retinoids by inducing expression of one or a plurality of the genes identified herein can be expected to have reduced or no such side-effects, making them better agents for anti-tumor and other therapies. Discovery of compounds that mimic the growth-inhibitory effects of retinoids without producing the toxic side effects of growth-inhibitory compounds known in the art is thus advantageously provided by the invention.

Please replace the paragraph at page 26, lines 18-22, with the following paragraph:

These sequences were then analyzed for the presence of two closely spaced hexameric core motifs of RARE sites (Mangelsdorf *et al.*, 1994, in THE RETINOIDS: BIOLOGY, CHEMISTRY, AND MEDICINE, (Sporn *et al.*, eds.), pp. 327-330 (Raven Press, New York), in variable orientations, using the "Regulatory Sequence Analysis Tools" available from the University of Brussels, Belgium.

Please replace the paragraph at page 28, line 10, to page 29, line 11, with the following paragraph:

The ability of this construct to drive retinoid-inducible luciferase expression in mammalian cells is demonstrated in transient transfection assay, as described in U.S. Provisional Patent Application Serial No. 60/265,840, filed February 1, 2001 and U.S. Patent Application Serial No. 09/861,925, filed May 21, 2001, incorporated by reference herein. Briefly, transfection is carried out using LIPOFECTAMINE 2000 (Life Technologies, Inc. Gaithersburg). Cells are plated at a density of 70,000 cells/well in 12 well plates in 1 mL media containing 2mM glutamine, 10% FBS; 0.1mM NEAA (Non-Essential Amino Acids, GIBCO), 1mM sodium pyruvate, and 10 μg/mL insulin, and without penicillin/streptomycin. After culturing the cells for a sufficient time that they attached to the culture dish, transfection was performed in triplicate according to the manufacturer's instructions, using 1 μg pGL2- basic vector DNA and 1 μg pGL2-βIG-H3 promoter DNA. After 10 hours, culture

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